UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, DC 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/702,114	08/23/96	IBEA M	1912-0151P

18N2/0513

BIRCH STEWART KOLASCH AND BIRCH
P O BOX 747
FALLS CHURCH VA 22040-0747

EXAMINER	
GUPTA,A	

ART UNIT	PAPER NUMBER
1811	6

DATE MAILED: 05/13/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

☆U.S.GOVERNMENT PRINTING OFFICE 1995-319-826

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	6

This is a communication from the examiner in charge of your application. DATE MAILED:
COMMISSIONER OF PATENTS AND TRADEMARKS

■ This application has been examined ☐ Responsive to communication filed on ____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 MONTHS from the date of this letter.
Failure to respond within the time period will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENTS ARE PART OF THIS ACTION:

1. ■ Notice of References Cited by Examiner, PTO-892.
2. ■ Notice re Patent Drawing, PTO-948.
3. ■ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ■ Claims 1-19 are pending in the application.
   Of the above claims, ____ are withdrawn from consideration.
2. ☐ Claims ____ have been cancelled.
3. ☐ Claims ____ are allowed.
4. ■ Claims 1-19 are rejected.
5. ☐ Claims ____ are objected to.
6. ☐ Claims ____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on ____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on ____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on ____ has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under 35 USC 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. ____; filed on ____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

08/702,114

DETAILED ACTION

Claim Rejections - 35 USC § 112
Second Paragraph

1. Claims 4-7, and 9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-7 and 9 is improperly dependent on base claim 2. Claim 4-7 and 9 recites that the sum of the variables to be lower than 5. However, base claim 1 recites that the sum of the variables can only be between 5 to 8.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-3, 9-10, and 12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gaudreau et al.

The prior art, on page 1866 table II, teaches a fatty body-hGRF(1-29)NH_2 moiety , compound number 4-8, that is encompassed by the claims, which help in increasing the hydrophobic character of the hGRF and induce GH secretion 2.4-12 fold.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless --**
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any

inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1 and 13-19 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gaudreau et al..

The claims are drawn to various method of uses for the GRF compound of claim 1.

The prior art, on page 1866 table II, teaches a fatty body-hGRF(1-29)NH_2 moiety , compound number 4-8, that is encompassed by the claims, which help in increasing the hydrophobic character of the hGRF and induce GH secretion 2.4-12 fold. The difference between the prior art and the instant application is that the reference does not teach a method of treating the disorders claimed. However, since the reference anticipates the compound of claim 1, the disclosed compound would inherently possess activity to treat the disorders of the method claims.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claim 1-10, 12, 14-15, and 19 are rejected under 35 U.S.C. § 103 as being unpatentable over Gaudreau et al. in view of Coy et al. in further view of Felix et al.

The claims are drawn to GRF peptides that have N-terminal modification in the form of hydrocarbon chain elongation of the N-terminus.

The reference of Gaudreu et al. teach the substitution of fatty body moieties linked at the N-terminal of the hGRF(1-29), as evident by Table II on page 1866. N-terminus elongation of hGRF by 4, 6, 8, carbon atoms increased the peptide hydrophobicity and induced GH secretion 2.4-12 fold. The reference of Coy et al. also teach that N-terminal acetylation were responsible for about a 12 fold increase in potency in the of the peptide (page 219). The difference between the prior art and the instant application is that the reference does not teach chain elongation of the N-terminus with alkenes.

However, as stated earlier the reference of Gaudreu et al. teach the elongation of the N-terminus by 4-8 carbons. Although the reference specifically teach the elongation by alkanes, one would expect that an alkene having 4-8 carbon atoms would be as effective in increasing the hydrophobicity of the peptide and induce GH secretion 2.4-12 fold. Therefore, it would have been obvious to acylate the fatty body at the N terminus of the hGRF because it is known that acylation at the N terminus of hGRF increases the potency of the peptide by a factor of 12 and thus helps in increasing the secretion of Growth Hormone. It would have been further obvious to substitute alkanes with the corresponding alkenes because one of ordinary skill would expect a similar result in the increase potency due to the close structural similarity between the two compounds.

It would have been obvious to acetylate a carbon chain either on a 29 amino acid GRF or a 44 amino acid GRF because both analogs have been demonstrated to have GH releasing activity.

As to the pharmaceutical formulations, the reference of Felix et al. teaches a pharmaceutical formulation for a GRF analog and the reference further states that GRF analogs are useful in treating dwarfism and promote wound healing (col. 1, lines 45-57).

5. Claims 1 and 13 are rejected under 35 U.S.C. § 103 as being unpatentable over Bercu in view of Gaudreau et al. or Coy et al.

The claim is drawn to a method of diagnoses of growth hormone deficiencies in patients, which comprises administering a GRF analog of claim 1.

The reference of Bercu teaches a method of diagnosing growth hormone disorders employing samatostatin and Growth Hormone Releasing Hormone. The method comprises inhibiting the secretion of growth hormone by administering somatostatin, stimulating the pituitary gland of growth hormone by administering Growth Hormone Releasing Hormone, monitoring the concentration of growth hormone in the bloodstream and finally classifying the individual as having a growth hormone deficiency upon the response. This reference further teaches that the Growth Hormone Releasing Hormone is also know as Growth Hormone Releasing Factor. The difference between the instant application and prior art is that the reference does not teach the use of the claimed GRF analogs.

However, it would have been obvious to one of ordinary skill in the art to use GRF analog of claim 1 as the Growth Hormone Releasing Factor of Bercu because the claimed GRF analogs are disclosed as old in Gaudreau et al. or Coy et al. and are also shown to stimulate growth hormone release. The substitution of the GRF analogs of Gandreau et al. or Coy et al. for those of Bercu would have been obvious to those skilled in the art given the close structural similarity and activity and accordingly, one would have reasonably expected to stimulate growth hormone release as suggested by the references.

6. Claims 1 and 17 are rejected under 35 U.S.C. § 103 as being unpatentable over Gaudreau et al. in view of Kann et al.

The claim is drawn to a method of improving protein anabolism which comprises administering a GRF analog of claim 1.

The prior art of Gaudreau et al., on page 1866 table II, teach a fatty body-hGRF(1-29)NH_2 moiety , compound number 4-8, that is encompassed by the claims, which help in increasing the hydrophobic character of the hGRF and induce GH secretion 2.4-12 fold. The difference between the prior art and the instant application is that the reference does not teach improvement of protein anabolism.

However, the reference of Kann et al. teaches a correlation between stimulation of protein anabolism and GRF (see col. 2, liens 1-11). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to improve protein anabolism with GRF because the reference of Kann et al. establishes a correlation between the stimulation of protein anabolism due to growth hormone secretion.

7. Claims 1 and 16 are rejected under 35 U.S.C. § 103 as being unpatentable over Gaudreau et al. in view of Recker.

The claim is drawn to a method of treating osteoporosis which comprises administering a GRF analog of claim 1.

The prior art of Gaudreau et al., on page 1866 table II, teach a fatty body-hGRF(1-29)NH_2 moiety , compound number 4-8, that is encompassed by the claims, which help in increasing the hydrophobic character of the hGRF and induce GH secretion 2.4-12 fold. The difference between the prior art and the instant application is that the reference does not teach the treatment of osteoporosis.

However, the reference of Recker et al. teach a method of treating osteoporosis by administering a GRF analog. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat osteoporosis with GRF.

8. Claims 1 and 18 are rejected under 35 U.S.C. § 103 as being unpatentable over Gaudreau et al. in view of Clark.

The claim is drawn to a method of inducing lipolytic effect which comprises administering a GRF analog of claim 1.

The prior art of Gaudreau et al., on page 1866 table II, teach a fatty body-hGRF(1-29)NH_2 moiety , compound number 4-8, that is encompassed by the claims, which help in increasing the hydrophobic character of the hGRF and induce GH secretion 2.4-12 fold. The difference between the prior art and the instant application is that the reference does not teach the inducing lipolytic effect.

However, the reference of Clark et al. teach a correlation between GH and lipolytic effect in animals (see col. 2, lines 41-66). Therefore, it would have been obvious to one of ordinary skill in the art that administration would result in the inducement of a lipolytic effect because administration of GRF results in GH secretion which in turn stimulates lipolytic effect.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (703) 308-0254. The fax phone number of this group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta

CECILIA J. TSANG
SUPERVISORY PATENT EXAMINER
GROUP 1800